

*In the specification:*

Applicants have added a paragraph on the Related Applications to the above-referenced application.

Applicants have amended the specification to correct typographical errors. No new matter has been introduced.

*In the claims:*

Claims 51-94 are pending in this application. The limitation found in dependent Claim 57 has been incorporated into amended claim 51. As such claim 57 has been canceled. Claims 51, 61, 65, 84, 91 and 94 have been amended. Support for the amendments can be found throughout the specification including for example at page 46, lines 1-5 ("inhibiting humoral immune response") and page 22, lines 19-31 ("disrupting the association"). As such no new matter has been introduced.

Rejection Under 35 U.S.C. § 112 Second Paragraph

Claims 51, 61, 65, 84, 91 and 94 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

- A. Claims 51 and 61 and claims 84, 91 and 94 have been objected to under 35 U.S.C. § 112, second paragraph as indefinite in the recitation of "altering". Applicants have amended claims 51 and 61 by replacing "altering" with "inhibiting" as described for example in the specification at page 46, lines 1-5 and page 65 in original claim 16 and have amended claims 84, 91 and 94 by replacing "altering" with "disrupting" as described for example in the specification at page 22, lines 19-31.
- B. Claims 84, 91 and 94 have been objected to under 35 U.S.C. § 112, second paragraph as ambiguous in that the Examiner asserts that it is not clear what sort of association of immune complexes and B cell follicles are altered and in what way. As described above, Applicants have amended claims 84, 91 and 94 by replacing the word "altering" with "disrupting" as described for example in the specification at page 22, lines 19-31. Moreover, Applicants provide below an explanation of the way the association of immune complexes and B cell follicles are altered. As such Applicants respectfully request that the 35 U.S.C. § 112, second paragraph rejection be withdrawn.

- C. Claims 51 and 61 have been objected to under 35 U.S.C. § 112, second paragraph as unclear with regard to whether “altering the [humoral] immune response” is the same as or related to the phrase therapeutically effective and how the therapeutically effective is connected to the preamble of “altering the [humoral] IR”. As amended the claims are now directed at inhibiting the humoral immune response. In order to address the Examiner’s question regarding the relation between altering (or rather inhibiting the humoral immune response) and its relation to a therapeutic effect Applicants provide the following explanation which is based on common facts known to those of skill in art:

Treatment of mice with LT $\beta$ R-Ig results in the disruption of the follicular dendritic cell (FDC) networks. FDCs are the only cells able to retain intact antigen as immune complexes on their surface via special receptors. B cells expressing high affinity surface immunoglobulin (sIg) which are capable of binding to the immune complexes deposited on FDCs are given positive survival signals and are ultimately selected into the memory B cell compartment. However, in certain humoral diseases, B cells that express sIg that recognizes self, as well as foreign antigen, may also be positively selected based on their ability to bind immune complexes on FDCs. Consequently, administering LTBR-Ig which disrupts the FDC network in these situations is beneficial since it prevents the selection of B cells expressing autoreactive Ig and ultimately decreases any associated pathology. Furthermore, it has been demonstrated that the disruption of the FDC network only delays normal foreign antigen humoral responses and does not completely abolish them, consequently suggesting that foreign antigen driven immune responses can be regulated by alternative selection mechanisms that are not available to self-antigen driven immune responses.

In view of the above, Applicants respectfully request that the 35 U.S.C. § 112, second paragraph rejection be withdrawn.

#### Rejection Under 35 U.S.C. § 112 First Paragraph

Claims 51-56, 58-70 and 84-94 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that while the specification is enabling for inhibition of immune responses as determined by the decrease in Ig levels, it does not provide enablement for “altering” responses wherein the altering may be an increase in the immune response.

Applicants have amended the claims by replacing "altering" with either inhibiting or disrupting. As such Applicants respectfully request that the rejection be withdrawn.

The Examiner also alleges that there is no guidance in the specification with respect to determining the association of immune complexes with B cell follicles. Applicants refer the Examiner to the explanation provided above for the rejection under 35 U.S.C. § 112 second paragraph.

With the amendment to the claims and the arguments provided above, it is respectfully requested that the rejections under 35 U.S.C. § 112 first paragraph be withdrawn.

#### Drawing Informalities

Applicants will submit replacement drawings upon receipt of a Notice of Allowance for the above-referenced case.

#### Conclusion

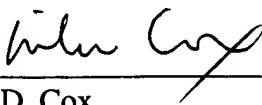
In view of the above argument, and the amendments to the claims, allowance of each of the pending claims as amended herein is earnestly solicited. If the Examiner believes that a telephone conference would expedite the prosecution of this application, please call the undersigned at (617)-679-2079.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 02-2327. However, the Assistant Commissioner is not

authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Date: 4/16/02

  
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